Radiocontrast Nephropathy

Troy M. DeNunzio, DO, CPT, MC

Nephrology Fellow

Walter Reed Army Medical Center

Objective

- Define radiocontrast nephropathy
- Diagnosis and clinical course
- Discuss incidence and risk factors
- Describe pathogenesis
- Treatment

Definition:

- An acute impairment of renal function that follows exposure to radiographic contrast (RC) materials and for which alternative etiologies have been excluded.
- A functional definition varies among different studies

  Most commonly reported as a rise in serum creatinine > 25% above baseline or an absolute rise of 0.5mg/dl within 48 hours after exposure to RC.

Clinical Presentation and Diagnosis

- Acute rise in serum creatinine within 24-48 hours after contrast administration. Peak at 4-5 days and returns to baseline over 7-10 days.
- Serum markers normal
- Usually non-oliguric
- Urinalysis: coarse granular casts, RTE and amorphous sediment. May have low grade proteinuria. Hematuria is absent. Urate and calcium oxalate crystals may be present.
- Fractional excretion of sodium may be < 1%
- Alternative etiologies are eliminated (i.e. atheroemboli, prerenal, sepsis, AIN).

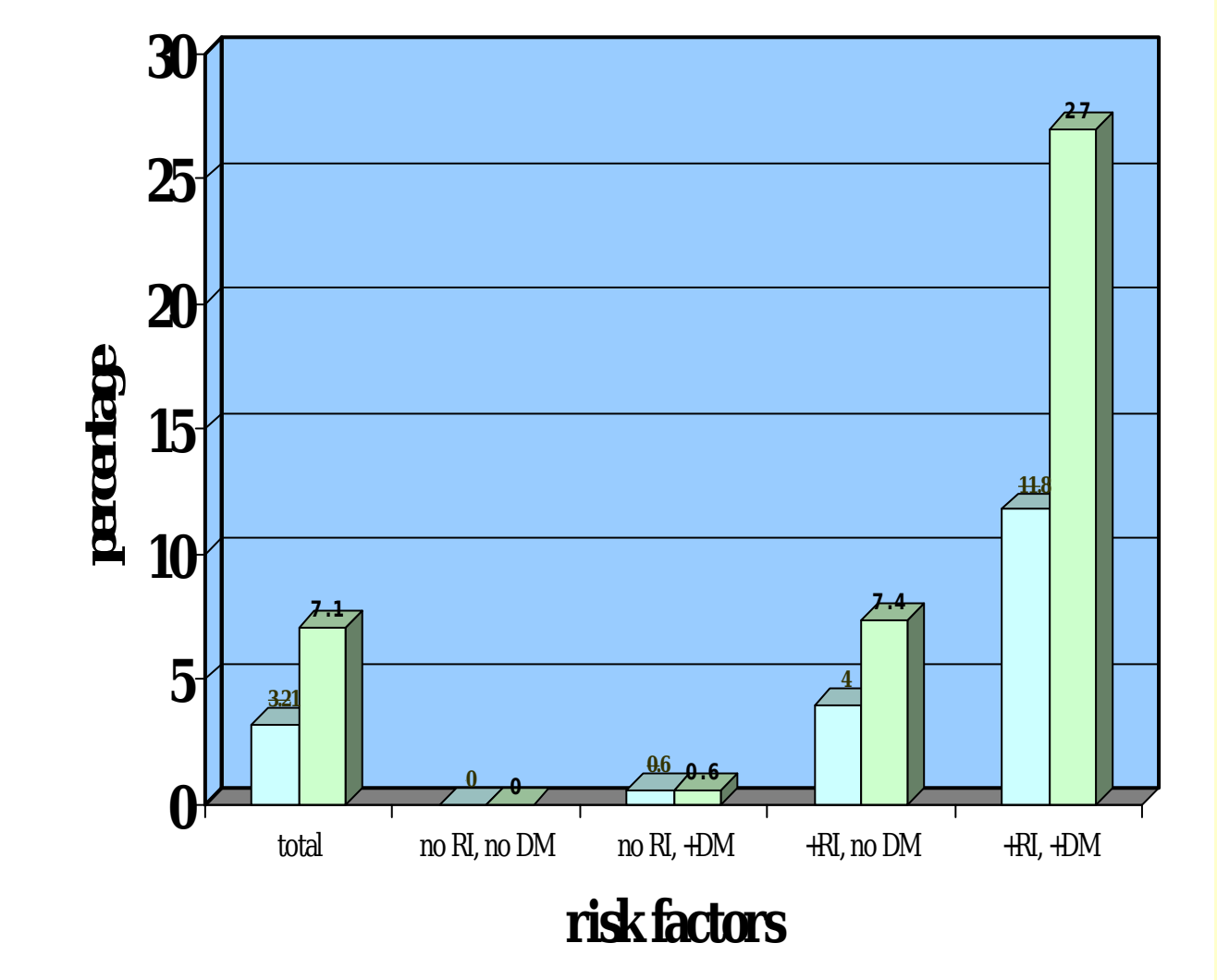
Incidence and Risk Factors

- Davidson et al (Annals of Internal Medicine 1989;110:119)
  - studied 1144 patients undergoing cath. All received IV fluid
  - mean baseline serum creatinine 1.02 mg/dl
  - 6% had RCIN (rise in cr. >0.5mg/dl)
  - 10.9% if baseline cr. >1.06mg/dl vs. 4.2% if < 1.06
  - no patient had anuria or required HD
  - risk factors: baseline serum creatinine and age
- Schwab et al (NEJM 1989;320:149)
  - 443 pts with baseline serum cr. 0.5-6.1 mg/dl undergoing cardiac catheterization. 235 HOCM and 208 LOCM. All hydrated
  - 160 pts were considered high risk (DM,CHF, or CRF)
  - overall 10.2% HOCM and 8.2% in the LOCM group had RCIN
  - 17% in HR and 15% in the LR categories, no HD or oliguria
  - the only independent predictor of RCIN was baseline serum creatinine

Incidence and Risk Factors

- Rudnick et al (KI 1995;47:254) prospectively studied 1196 patients undergoing cardiac cath.
  - divided on the basis of RI and DM and they were randomized to receive either LOCM or HOCM
  - all were prehydrated. RI was determined on by serum cr. > 1.5 mg/dl
  - logistic regression analysis determined that significant RF for RCIN
    - baseline RI (serum cr. >1.5 mg/dl) **RR 21.1**
    - DM, **RR 3.4**
    - male gender
  - 15/61 patients with nephrotoxicity had serious outcomes (oliguria, requirement for HD, or increase in cr. High enough to consider HD)
    - 80% were male and baseline creatinine in all was 2.7mg/dl
    - 66.6% NYHA II,IV, 73% DM
    - 8 req. HD. No difference in contrast agent

Rudnick et al (KI 1995;47:254) percentage of patients with RCIN (>50 % increase in serum creatinine or 1.0mg/dl)



Frequency of Nephrotoxicity

defined as increase in serum creatinine >0.5mg/dl by treatment stratification group

	Nonionic	Ionic
Group	n/N (%)	
(-) RI (-)DM	16/188 (8.5)	14/171 (8.2
(-) RI (+)DM	11/153 (7.2)	18/162 (11.1)
(+) RI (-)DM	18/148 (12.2)	40/148 (27.0)
(+)RI (+)DM	34/102 (33.3)	53/111 (47.7)
Total	79/591 (13.4)	125/592 (21.1)

Incidence and Risk Factors

- Barrett et al (KI 1992;41:1274) specifically looked at pts with renal insufficiency.
- 249 with serum creatinine >1.35mg/dl, receiving either cardiac cath or contrast CT.
- received either LOCM or HOCM

RCIN	HOCM	LOCM
>25% inc. in serum cr	6.8%	3.8%
>50% inc	3.4%	1.5%

- RCIN correlated only with pre-contrast creatinine and DM

Incidence and Risk Factors

Barrett et al (KI 1992;41:1274)

- When stratified according to RF the risk for RCIN:

no DM, serum cr. >1.5 , <2.35	16/266 (6%)	type of contrast NS
+ DM, serum cr. >1.5 , <2.35	4/36 (11%)	
no DM, serum cr. >2.35	8/48 (16.7%)	
+ DM, serum cr. >2.35	5/13 (33%)	

Incidence and Risk Factors

- Weisberg et al (KI 1994; 45:259) studied the risk of RCIN in patients with and without DM and with CRI undergoing cardiac cath.
  - 50 pts; 24 DM and 26 no DM
  - 15 patients received saline alone
    - 7 DM, baseline serum cr. 3.1, RCIN 43%
    - 8 no DM, baseline serum cr. 2.3, RCIN 38%
  - overall 19/50 had RCIN, 16/19 had DM, RR 5.78
- Solomon et al (NEJM 1994;331:1416) also performed a study patients with CRI undergoing cardiac cath.
  - 78 pts with mean s. cr. 2.1 mg/dl
  - 26% overall RCIN
    - 3/28 (11%) in saline only
    - 2/3 had inc. of creatinine from 3.5-5.0
  - significant risk factors were baseline creatinine, DM and CHF

Incidence and Risk Factors

- Moore et al (Radiology 1992;182:609)
  - 929 patients either CT or angiogram, HOCM or LOC
  - 35 % of pts with s. cr. >1.5mg/dl

	Total	CT	Angio
LOM	2.7%	1.2	4.4
HOM	2.9%	2.0	4.0

  - Independent risk factors:
    - IDDM, RR 3.0
    - serum creatinine >1.5mg/dl, RR 3.5
    - IDDM + RI, RR 9.2
    - NYHA class II or IV CHF, RR 12.0

Incidence and Risk Factors

- Stevens et al (JACC 1999;33:403) studied 98 patients undergoing cardiac catheterization, 55 received only IV fluids
  - Baseline serum creatinine 2.55 +/- 0/91 mg/dl
    - 17/55 (30.9%) had >25 % rise in creatinine
    - 10/55 (18.2%) had serum cr. Inc. to >5.0 mg/dl
    - 5/55 req. Hemodialysis

- Erley et al (Nephrology, Dialysis, Transplant 1999;14:1146)
  - 80 pts with serum cr. >1.5 undergoing cardiac cath.
  - All received IV hydration and low osmolar agents
  - 1/29 RCIN

Incidence and Risk Factors

- Lautin et al (American Journal or Radiology 1991; 157:49)
  - reported
    - 10 % overall for non-azotemic pts
    - 2 % for non diabetics
    - 16 % for diabetics
    - 30 % for azotemic pts.
    - 38% for azotemic pts with DM

- Parfrey et al (NEJM 1989;320:143)

DM/ non-azotemic:	0/85 (had >50% inc. in serum cr.)
	2/85 (had >25% inc. in serum cr.)
DM/azotemic	3/34
	3/34
no DM/azotemic	4/101(4%)
	6/94 (6%)

Incidence and Risk Factors

- Manske et al (American Journal of Medicine 1990;89:615)
  - studied 59 patients with IDDM and a mean serum creatinine of 5.9 mg/dl
  - all were undergoing coronary angiogram for pretransplant evaluation
  - 50% had RCIN (serum cr. Inc. >25% above baseline)
  - 9/59 required hemodialysis; 5 long term
  - significant RF was the amount of contrast dye
- Wenrauch et al (Annals of Internal Medicine 1977; 86:56)
  - studied 13 juvenile patients with IDDM receiving cardiac cath for transplant evaluation; mean cr. 6.8 mg/dl
  - 12/13 RCIN
  - 9/12 were initially oliguric, 7 req. HD, 4 long term

Incidence and Risk Factors

- Multiple Myeloma is not significantly associated with RCIN
- McCarthy et al (Radiology 1992;183:519)
- Performed a literature review of 7 studies which included 476 patients.
- Incidence ranged from 0.6-1.25 %
- All studies reported that patients received adequate hydration

Incidence and Risk Factors Summary

- Incidence:
  - nl renal function 0-4.2 %
    (with or without DM)
  - mild to moderate RI 4-38%
    (cr. >1.5-5.0)
  - mild to moderate RI 10-47%
    with DM
  - severe RI (cr. >5.0) 50-92 %
    - risk for HD 15-53%
    - risk for long term HD 8-33%

Incidence and Risk Factors Summary

- Risk factors:
  - prexisting renal insufficiency
    - RR 3.5-21
  - Diabetes
    - RR 3-5.78
  - RI+DM
    - RR 9.2
  - CHF (NYHA III,IV)
    - RR 12.0
  - age, male gender

Pathogenesis

- Altered glomerular hemodynamics
  - direct vasoconstriction-endothelin
  - prostaglandin/NO synthesis inhibition
  - disturbance of tubulo-glomerular feedback
    - adenosine
- Direct cell injury
  - reactive oxygen radicals
  - obstruction/Tamm-Horsfall proteinuria
  - alteration of tight junction proteins

Porter and Kremer, Clinical Nephrotoxins 1998: pp317-321

Pathogenesis

- Renal medulla functions normally on the verge of hypoxia, with PO_2 as low as 20mmHg
- medullary blood flow represents only 5-10%of renal blood flow and is further compromised by shunting within the vasa recta from the afferent to the efferent limb.
- O2 supply and demand are maintained in delicate balance
- a decrease in blood flow or an increase in solute delivery can cause a negative 02 balance.
- Both mechanisms are thought to contribute to negative O2 balance, decrease in GFR , and ultimately ischemic necrosis of the outer medullary tubule,which is the histologic hallmark of radiocontrast -induced nephropathy.
- Decreased blood flow results altered renal hemodynamics after exposure to RC.

Altered renal hemodynamics

- The renal vascular response to radiocontrast agents is thought to be biphasic.
- There is an initial period of vasodilatation with augmented renal blood flow that lasts minutes to hours, followed by a period of prolonged vasoconstriction. This is largely based on results of animal studies (Agmon et al JCI 1994; 94:1069)
- The initial response was clearly demonstrated in humans by Weisberg et al (KI 1992; 41:1408, KI 1994; 45:259).
- The subsequent vasoconstriction in humans is less clearly demonstrated.
  - Erley et al (KI 1994; 45:1425) showed only a modest decline in RPF at 4 hr after contrast exposure.
  - Deray et al (Clinical Nephrology 1991;36:93) demonstrated these effects over a more prolonged period.
  - most of the vasoconstrictive effects are presumed on the basis of reductions of GFR measured with Inulin, or by reductions of creatinine clearance that occur subsequent to contrast exposure.

Altered renal hemodynamics-Endothelin

- Endothelin is a potent endogenous vasoconstrictor released from endothelial cells.
- Radiocontrast agents directly cause release of endothelin from cultured endothelial cells. (Heyman et al JASN 1992; 3:58)
- Endothelin levels increase in the blood of patients exposed to RC , usually at the time of the observed decrease in RBF (Marguiles et al JASN 1991; 2:1041).
- Endothelin levels are higher after the exposure to high osmolar contrast agents than to low osmolar compounds.

Altered renal hemodynamics-Endothelin

- Clark et al (AJKD 1997;30:82) demonstrated that exposure to iopamidol (LOCM) induced significant increases in endothelin-1 levels in normal human subjects during cardiac catheterization. In patients with either CRF or DM the increase was even more pronounced.

- Cantley et al (KI 1993; 44:1217) showed that RBF was decreased to 80% of baseline after RC exposure and that this response could be attenuated with ET-1 blockade. The inhibition of cyclo-oxygenase prior to contrast exposure induced an even more pronounced decline in RBF which was also attenuated with ET-1 blockade. This suggests a role for both renal prostaglandins and endothelin in RCIN

Altered renal hemodynamics-Adenosine

- Oswald et al (KI 1991;32 S1:128) showed in an animal model that if renal blood flow is diminished the vascular response post-obstruction is additional vasoconstriction. This response is attenuated by theophylline.
- Dipyridamole, which enhances extracellular release of adenosine, potentiates this vasocontrictor response.
- Increasing NaCl delivery to the macula densa also results in increased adenosine release.
- Erley et al (KI 1994;45:1425) showed that in patients with and without CRI that RC induced a decrease in GFR that could be suppressed with theophylline
- Later studies by this same group in both rats and humans suggested that only in the setting of volume depletion was theophylline of any benefit (Erley et al NDT 1999;14:1146, KI 1998;67:S192)

Prostaglandins/NO

- Most animal models use pretreatment with a cyclo-oxygenase (CO) inhibitor to induce RCIN
- Renal PG's and NO are counter-regulatory vasodilators to renal vasoconstriction.
- RCIN is uncommon in normally functioning kidneys
- In studies of animals with normal renal function, inhibition of CO causes decreases in RBF and GFR after the exposure to RC.
- When renal function is impaired there is a more severe response.
- There are no human studies that actually have demonstrated these effects in humans, but in disease states where impaired production PG's are presumed there is increased incidence of RCIN
- the role of renal prostaglandins is therefore inferred from this data.

Prostaglandins/NO

- Inhibition of NO synthesis, which is a renal protective vasodilator, predisposes to RCIN.
- Agmon et al (JCI 1994; 94:1069) studied the effects of RC on a rat model in which NO synthesis was inhibited by L-name.
- After exposure to iothalamate medullary blood flow increases
- Pretreatment with L-name attenuates this response. A decline in RBF and GFR occur and there is mild ischemic necrosis.
- This effect is exacerbated when indomethicin was additionally applied.
- Conclusion: NO and PG's have a renal protective effect and that impaired production predispose to RCIN.
- This is extrapolated to humans, whereby in those disease states where NO is thought to be impaired, there is increased incidence of RCIN. This is postulated but not proven mechanism in RCIN.

Direct Tubular injury: reactive O_2 species

- Pretreatment of the rat model of RCIN with catalase or superoxide dismutase is protective against ischemic injury.
- Barkis et al (AJP 1990; 258:F115) reported an increase in reactive oxygen species when human mesangial cells were exposed to RC.
- Toshima et al (KI 1994; 41:1008) demonstrated that water deprived rats exposed to RC had decreased activity of catalase and superoxide dismutase compared to volume replete rats and significant decline in GFR. If they were pretreated with catalase the effects were attenuated and if volume was restored they were completely suppressed.

Direct Tubular injury

- Brush border enzymes, small molecular weight proteins and lysozymal enzymes appear in the urine following exposure to RC. Although they suggest tubular injury they have not been significantly associated with RCIN
- Tamm-Horsfall proteins have been demonstrated to have increased urinary levels following RC. It has been suggested that they might coprecipitate with filtered contrast and lead to obstruction. Again, this has never been proven.
- Finally, Schick et al (NDT 1999;14:312) demonstrated that HOCM produce direct cytotoxic effects on renal epithelial cells in vitro. After exposure of canine renal tubular cells to HOCM they were able to demonstrate redistribution of the tight -junction associated proteins into the cytosolic compartment

Treatment

- Vasodilators
  calcium channel blockers
  atrial natriuretic peptide
  dopamine
  theophylline
- High osmolar vs. low osmolar agents
- Hydration
- Diuretics
- Hemodialysis

Calcium Channel Blockers

- Cacoub et al. (Clinical Nephrology 1998; 29:215) evaluated 27 patients with moderate renal insufficiency (baseline cr. Clearance 20-60 ml/min)
  - pts received either nifedipine 40mg/day or no CCB and all received radiocontrast (RC) agents for various reasons.
  - 36% of patients in the CCB group and 37.5% in the control group experienced radiocontrast-induced nephropathy (RCIN), defined as a 20 % increase in serum creatinine over baseline.
  - There was no mention of underlying disease or hydration status.

Calcium Channel Blockers

- Russo et al (Nephron 1990;55:254)

  prospectively studied 20 pts, undergoing IVP. 10 pts received 10 mg of sublingual nifedipine and 10 placebo.
  - Prior to the study all patients received IV hydration and had a GFR of at least 100 ml/min.
  - GFR, and RPF were measured at the start and at 1, and 2 hours after contrast administration.
  - In the CCB group at 1 and 2 hours both the GFR and RPF were 40-60 % above baseline.
  - In the control group all had a modest decrement in both measurements.
  - Renal function was not measured at 1-2 days when clinically significant RCIN occurs and there was no mention of patient demographics.

Calcium Channel Blockers

- Neumeyer et al (Nephrology, Dialysis, Transplant 1989; 4:1030) randomized 35 patients to receive either nitrendipine or placebo prior to radiocontrast.

	precontrast GFR	2 days post GFR	
CCB (n=16)	64.7 ml/min	64.6	
placebo (n=19)	82	62	(dec. 26.7%)

- Suggests a possible benefit in patients with mild renal impairment. However, these patients were not hydrated.

Dopamine

- Hans et al (Radiology 1990; 176:651)
- Randomized 60 patients to receive a dopamine infusion (2.5 mcg/kg/min) or placebo prior to arteriogram.
- All patients had serum creatinine 1.3-3.5, 50% were diabetic
- All received high osmolar agent and IV hydration.
- In the control group, creatinine clearance (by inulin) decreased from 48 to 37 ml/min after 24 hours but returned to baseline at 48.
- There was no change in creatinine clearance in the dopamine group.
- There was no subgroup analysis of the patients with DM.

Dopamine

- Hall et al (Journal of Surgical Research 1992; 53:317)

  Studied the effects of renal dose dopamine (3 mcg/kg/min) administered prior to angiogram, in patients with serum creatinine >2.0 mg/dl.
- All patients received adequate hydration.
- 11 patients received dopamine and none had an increase in serum creatinine after contrast.
- 8/13 patients receiving only IV fluids had an increase in creatinine, with a mean rise for the group from 2.6 to 3.9 mg/dl.
- One patient in the latter group required HD.
- There was no difference among DM and non-DM.
- This study suggests a possible benefit of low-dose dopamine in patients with moderate renal insufficiency.

Dopamine

- Weisburg et al (KI 1994; 45:259) specifically studied the effects of RC in diabetics with mild to moderate renal insufficiency.
- 50 pts; 24 DM, avg. s. cr. 2.6 and GFR 32ml/min
  26 non-DM s. cr. 2.4 and GFR 34ml/min

- 7 patients with DM received dopamine and 83% experienced RCIN
- 8 patients without DM received only saline and none had RCIN
- The mean RBF was lower in the DM group, but increased significantly after dopamine infusion.
- The decline in renal function in the dopamine group was presumed to have been an effect of an intrarenal steal phenomena which causes worsening perfusion to the medullary tissue.
- A protective effect is noted in the non-diabetic group, suggesting a benefit similar to that noted in the Hall study.

Dopamine

- Gare et al (JACC 1999;34:1682) studied 66 patients with DM and underlying renal insufficiency.
- All pts received D51/2 NS @100 ml/hr for 12 hours before and up to 36 hrs after cardiac catheterization and all received low osmolar contrast.
- Dopamine group:
  - 33 pts had DM and mild renal insufficiency creatinine 1.2-2.2, with 10 patients with cr. 1.5-2.2.
  - rise in creatinine was 2, 10 and 13 % above baseline at 1,2 and 5 days post cath. 4 patients had RCIN (<40% increase in s. cr.)
- Control (saline only):
  - 33 pts had DM and mild renal insufficiency,creatinine 1.2-2.2, with 12 patients with cr. 1.5-2.2.
  - Rise in creatinine was 0, 2 and 17 % on days 1, 2, 5 post cath. 2 patients had RCIN (<40% increase in s. cr.)

- There was no statistical difference among any group suggesting that there is no advantage of dopamine over saline alone.

Theophylline

- Erley et al (KI 1994; 45:1425) studied 39 pts. receiving a low osmolar contrast. They were randomized to receive either oral theophylline(TP) or placebo(Plac)

	GFR (ml/min)		Creatinine clearance(ml/min)	
	before	4 hr	before	2 days
TP (19)	75	78	72	67
<75ml/min	54	57	46	45
Plac (20)	88	75 *	89	66*
<75ml/min	55	47 *	39	29

* significant

- Suggests that there may be a mild benefit in patients with mild renal insufficiency

Theophylline

- Katholi et al (Radiology 1995;195:17) studied 93 pts. Exposed to RC, either high or low osmolar and given either theophylline or placebo. All pts received hydration over 3 days and 90% were on CCB.

	Creatinine Cl (ml/min)			Serum cr (mg/dl)	
	baseline	24 hr	48	baseline	48 hr
HOCM					
TP(23)	80	61	62	1.2	1.3
PL(22)	79	46	43	1.2	1.3
LOCM					
TP(24)	80	81	81	1.3	1.3
PL(24)	82	68	81	1.2	1.2

Theophylline

- Erley et al (NDT 1999; 14:1146)
  - Examined the effect of oral theophylline vs. IV hydration in patients with baseline serum creatinine >1.5 mg/dl
  - 80 pts: all treated with IV hydration and 40 with oral theophylline.
  - All pts exposed to LOCM
  - 5.7% of pts with TP had RICN
  - 3.4% pts with hydration alone
- Conclusion: theophylline is not superior to IV hydration alone.

Atrial Natriuretic Peptide

- Weisburg et al (KI 1994; 45:259)
  - Studied the effects of ANP in a small group of patients with chronic renal insufficiency, with and without DM, that underwent cardiac catheterization.
  - All were hydrated with .45% saline at 100ml/hr for 12 hours before and during the procedure
  - Prior to the study all patients with DM had decreased renal blood flow. After the administration of ANP and contrast RBF increased.
  - 83% of diabetic patients experienced RCIN compared to 0% in the control group.
  - This suggest a possible role for ANP in patients with moderate renal insufficiency.
  - This study consisted of only 10 patients and therefore lacked sufficient power to be predictive of a larger population.

- There are no other significant studies of ANP.

High vs. Low Osmolar agents

- Harris et al (Radiology 1991; 179:849) randomized 100 pts with serum creatinine 1.4-2.4 undergoing CT scan to either a high or low RC. RCIN was defined as an inc. cr >25% above baseline
  - 7/50 HOCM had RCIN
  - 2/50 LOCM RCIN
  - 3/7 in the HOCM group had DM and none in the LOCM

- Schwab et al (NEJM 1989;320:149)
  - randomized 443 pts into high risk vs. low risk based on the presence DM, CHF or CRF.
  - randomized them to receive either a HOCM or LOCM.
  - LOCM: 8.2 %RCIN total with 15 % of those at high risk
  - HOCM 10.2%RCIN total, 17%of those at high risk
- No statistical difference in any group regardless of agent used or the presence or renal insufficiency (cr. >1.5)

High vs. Low Osmolar agents

- Barrett et al (Radiology 1993;188:171)
- performed a meta-analysis of 25 trials that examined the incidence of RCIN among patients receiving LOCM vs. HOCM
- with available data up to 1991 the odds ratio of a rise in serum creatinine of more than 0.5 mg/dl with LOCM was 0.61
- In subgroup analysis:
  - patients with preexisting renal failure (serum creatinine >1.4 mg/dl or GFR <70 ml/min) the odds ratio of RCIN for LOCM 0.5
  - and those without renal failure was 0.75

High vs. Low Osmolar agents

- Rudnick et al (KI 1995; 47:254) provided one of the largest studies comparing these 2 agents. They compared 1196 pts. undergoing cardiac cath. who received either iohexol(LOCM) and diatrizoate(HOCM).

	Nonionic	Ionic
Group	n /N (%)	
(-) RI (-)DM	16/188 (8.5)	14/171 (8.2)
(-) RI (+)DM	11/153 (7.2)	18/162 (11.1)
(+) RI (-)DM	18/148 (12.2)	40/148 (27.0)
(+)RI (+)DM	34/102 (33.3)	53/111 (47.7)
Total	79/591 (13.4)	125/592 (21.1)

- In patients with normal renal function with or without DM had no significant difference. However, in patients RI there was a significant difference in the incidence of RCIN.

Hydration and Diuretics

- Solomon et al (NEJM 1994; 331:1416) studied the effects of saline, mannitol and furosemide in patients undergoing contrast studies.
- 78 pts, all with CRI and a baseline creatinine of 2.1
- all patients received 1/2 NS for 24 hrs periprocedure
- 68% LOCM, 32% HOCM
- 20/78 RCIN, 50% had DM but did not have a SS increased incidence.
  - 3/28 (11%) pts with saline alone
  - 7/25 (28%) with mannitol
  - 10/25 (40%) with furosemide all with significant inc. over control
- Suggests that in pts with moderate renal impairment, the incidence of RCIN is low with saline alone and diuretics may actually be deleterious

Hydration and Diuretics

- Stevens et al (JACC 1999; 33:403) recently performed a similar study in 98 pts. Undergoing cardiac cath with renal dysfunction

	serum cr.(mg/dl)		Increase in serum cr.		
	Base	48hr	%>25%	>100%	cr >5 mg/dl
control n=55(31 DM) (1/2ns @150ml/hr)	2.55	3.06	17(30.9%)	3.6%	10 (18%), 5/10 with DM
treat: n=21(11DM) fluid,lasix,dopamine	2.65	3.21	7(33%)	0	3 (14.3%) 1/3 DM
treat: n=22(10DM) fluid,lasix,dopamine, mannitol	2.2	2.72	7(31.8%)	1(4.5%)	2 (9.1%) 1/2 DM

- difference for DM was not significant.. Incidence of RCIN is high in all groups. No advantage to diuretics over saline alone and either diuretic did not increase the risk as in the Solomon study(this may be a result of the effect of dopamine.

Role of Hemodialysis

- How effectively does HD remove contrast dyes
  - Evans et al (J Clinical Pharm 1988) studied plasma clearance of iothalamate in 7 pts with ESRD on HD.
    - Plasma clearance 104 ml/min, with approximately 69% removed after 4hr of conventional HD.
    - Plasma osmolality had no significant increase, avg 294 before and 302 after.
    - ECF fluid shift after 2.1 mg/kg dye load (osmolarity 1483mmol/L) was estimated to theoretically to expand the intavascular volume 323 ml. However, only about half of this actually occurred.
  - Moon et al (Nephron 1995;70:430) studied the effects of HD on 7 pts with ESRD and 13 with s. cr. avg. 4.6 mg/dl all treated with HD after contrast studies.
    - Iohexol clearance was 70.4 ml/min and approximately 70% was removed by a 6 hr HD session.
    - No further decline in renal function occurred in any pt. There was no control group
    - renal clearance, which generally approximates GFR, decreased to negligible during HD

Role of Hemodialysis

- Lehnert et al (NDT 1998; 13:358) also attempted to address the role of HD as prophylaxis against RCIN in patients with moderate-severe renal impaiment undergoing contrast studies.
  - 30pts with baseline cr. 2.4, randomized to receive either HD or conservative therapy (periprocedure fluid) after contrast
  - overall 47% RCIN
    - 8/15 without HD, 4 DM, 4 non-DM
    - 6/15 with HD, 3 DM, 3 non-DM
    - No significant difference
  - contrast elimination 89 % by 24 hr in the HD group vs. 83% in the control, (significant)

Alternative Agents: Gadolinium/CO_2

- Spinoza et al (Radiology 1999; 210:663, AJR 1999;173:1403)
- published 2 recent articles that discuss the use of either CO_2 or gadolinium during angiographic studies.
  - 25 patients with baseline serum creatinine 3.5 (1.8-6.9)
  - 23/25 had no change in serum creatinine at 48 hours, 1 patient had CES and 1 had acute renal allograft rejection
  - also retrospectively reviewed all the cases in their hospital (unpublished). No cases of renal failure with Gad or CO_2 vs. 23% with iodinated contrasts.
- Advantages : quality of images are approaching that of iodine studies. No evidence in the literature of renal failure in either animal or human subjects
- Disadvantages: expensive, overestimates findings
- Interestingly: the osmolality is a minimum of 789mosm/kg and 70% is renally excreted

Recommendations

- Patients with normal renal function with and without DM.
- Patients with mild to moderate renal insufficiency, with and without renal insufficiency.
- Patients with severe renal impairment or already on Dialysis

Recommendations

- patients with normal renal function with and without diabetes need no intervention other than ensure adequate hydration
- In patients with mild to moderately impaired renal function
  - discontinue NSAID and diuretics
  - Use Low osmolar compounds (cost is not an issue in this patient population, since in the inpatient setting increases length of stay and is associated with increase in morbidity and mortality)
  - no benefit or CCB, but would not add or subtract from medical regimen.
  - correct cardiac decompensation if possible
  - Hydration
    - overwhelmingly proven to be effective
    - most studies support 1/2 ns or D5 1/2 ns 24hrs periprocedure
      - no recs for outpatient regimen or support to justify admission
      - consider 3-4 hours @100ml/hr before and after (Solomon, Seminars in Nephrology,opinion)

Recommendations (cont.)

- no benefit to any diuretic regimen , dopamine or ANP
- consider theophylline if adequate hydration cannot be accomplished

- In patients with severe renal impaiment
  - treat with same principles as in moderate renal insufficiency
  - no benefit to prophylactic HD
  - HD may decrease residual renal function
- Patients with ESRD
  - no studies support the need for adjustment of HD scheduled

Conclusion

- Provided definition and diagnostic criteria
- Reviewed the incidence and significant risk factors
- Discussed current theory of pathogenesis.
- Treatment options and recommendations
- Introduced current concepts of preventative therapy